Title

Negative emotional stimulation decreases respiratory sensory gating in healthy humans.

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Abstract

We tested the hypothesis that negative emotions decrease the respiratory-related evoked potentials (RREP) sensory gating (RSG). RREP were elicited by paired inspiratory occlusions. RSG was calculated as the difference in the averaged RREP peak N1 amplitude between the second (S2) and the first occlusion (S1). RSG was compared between unpleasant and neutral emotional conditions elicited by viewing affective pictures from the IAPS system in thirteen healthy adults. Results are expressed as median [min;max]. Compared to neutral pictures, viewing unpleasant pictures decreased the RREP N1(S1) amplitude (-3.37 µV [-4.62;-1.37] versus -4.59 µV [-6.08;-1.36]; p=0.017) but not the RREP N1(S2) amplitude (-0.26 [-3.24;2.36] versus -0.7 [-1.54;3.6]; p=0.68), and reduced the difference score S2-S1 (3.73 µV [0;5.82] versus 4.79 µV [3;6.2]; p=0.038). We concluded that a negative emotional stimulation could attract subject's attention to the detriment of the respiratory sensory inputs and produced an overall decrease in the RSG. This latter finding might participate in an over-perception of repeatedly presented respiratory stimuli.

Key words

Emotion

International Affective Picture System

Dyspnea

Respiratory sensation

Respiratory related evoked potential

Sensory gating

1. Introduction

Sensory perception is the act of interpreting and organizing sensory information, or sensation, to produce a meaningful experience of the world and of oneself (De Ridder et al., 2011). The perception of respiratory sensations in particular functions to warn the organism that an unusual respiratory event has occurred. Thus, dyspnea, or unpleasant respiratory sensation (Parshall et al., 2012), should induce a strong alarm of respiratory difficulty resulting in breathing pattern changes and specific actions (von Euler, 1981). In asthma, for example, the perception of bronchoconstriction induces dyspnea, increases the respiratory rate (Tanaka et al., 1990) and leads patients to take rescue medication. However, the perceived respiratory sensation does not strictly correlate with the magnitude of the corresponding stimulus. This has been largely investigated in asymptomatic bronchial hyperresponsiveness (Brand et al., 1992) and asthma (Bijl-Hofland et al., 1999; Burdon et al., 1982; Dahme et al., 1996; Grazzini et al., 2002; Kendrick et al., 1993; Rubinfeld and Pain, 1976; Wamboldt et al., 2000), where a similar fall in the forced exhaled volume in 1 second (FEV1) provoked respiratory sensations of variable intensity. As no pulmonary physiological deficit could explain this variability (Boulet and Turcotte, 2007), subjects were categorized in over-, normo- and poor-perceivers (Boulet et al., 1994). Based on clinical and experimental observations (De Peuter et al., 2008; Giardino et al., 2010; Li and Puntillo, 2006; Livermore et al., 2008; Nardi et al., 2009; Spinhoven et al., 1997; von Leupoldt et al., 2006), the idea emerged that psychological factors could modify respiratory sensory perception (Boulet et al., 1991; Gibson, 1995). However, objective modulation of respiratory sensory processing by emotion has not been studied extensively. In the present study, we investigated the impact of experimentally elicited unpleasant and neutral emotions on the cortical neural processing of respiratory sensations.

The respiratory related evoked potential (RREP) is one of the neural correlates of respiratory sensory perception (Davenport and Vovk, 2009). The RREP is produced by a mechanical stimulus, such as an inspiratory load or an inspiratory occlusion (Chan and Davenport, 2010a). Activation of intercostal, diaphragmatic and upper airway mechanoreceptors produces an afferent neural signal that projects into the brain and is processed by subcortical and cortical structures (Chan and Davenport, 2010a; Davenport and Vovk, 2009; Donzel-Raynaud et al., 2004). The neural dipole potential derived from

the summed cortical activity, or RREP, displays three early peaks (Nf, P1 and N1) (Davenport et al., 1986) and two late peaks (P2 and P3)(Webster and Colrain, 2000b). The RREP is directly related to respiratory sensory perception in healthy subjects and in life-threatening asthma patients (Davenport et al., 2012; Davenport et al., 2000; Knafelc and Davenport, 1999). Emotion does not modify the amplitudes of the RREP early peaks (Von Leupoldt et al., 2010b) suggesting that affect does not act on respiratory perception by increasing the respiratory sensory-related discriminative cortical activity.

Neural gating is the brain mechanism to filter continuous sensory inputs before they reach high level cortical processes in order to suppress redundant or insignificant stimuli (Cromwell et al., 2008). This central neural process is present for most somatosensory modalities including respiratory sensations. Studying the respiratory sensory cortical gating requires the production of two successive and similar inspiratory occlusions within a single inspiration. The first inspiratory occlusion is thought to generate a memory trace to which the second is compared upon arrival. Processing of the second occlusion is then actively inhibited within a specific period (usually less than 1 second) as this repetition contains no new information. For gating of the RREP, the amplitude of the second stimulus-elicited N1 peak is lower than the amplitude of the first stimulus-elicited N1 peak (Chan and Davenport, 2008). We hypothesize in the present study that negative emotion can decrease the respiratory sensory gating. The effect of unpleasant emotion induced by affective pictures on the respiratory sensory gating was assessed using the RREP measure in healthy subjects.

2. Methods

2.1. Ethics

The study was approved by the Institutional Review Board at the University of Florida (IRB201300648). All participants received oral and written information and provided written informed consent to participate in the study.

2.2. Subjects

Spirometry was performed to exclude airway obstruction defined as a ratio FEV1/FVC less than 0.7. Anxiety state was assessed before the onset of the experiment by the State-Trait Anxiety Inventory questionnaire (Spielberger et al., 1970). State anxiety (anxiety just before the experiment) and Trait

anxiety (general anxiety) were scored from 20 (no symptoms) to 80 (maximum symptoms). Sixteen healthy adults (8 males and 8 females) participated in the study. Three of them were excluded because of airway obstruction in one case, failure to complete the experiment in one case and inappropriate emotional response to IAPS pictures in one case.

2.3. Procedure

Participants sat comfortably in a recliner located in a sound and light-attenuated room separated from the researcher. During the experiment, the researcher monitored the subject's behavior with a camera but no images were recorded. Participants breathed through a breathing circuit consisting of a mouthpiece, a pneumotachograph and a non-rebreathing valve. The inspiratory port was connected to an occlusion valve with reinforced tubing. A noseclip prevented nasal airflow. This breathing circuit allowed the application of inspiratory occlusions and the monitoring of respiratory pattern. The experiment included two emotional conditions, unpleasant and neutral, provoked by watching affective pictures from the International Affective Picture System (IAPS) (Lang, 2008). A 5-minute break separated the two experimental conditions. The condition order was randomized. Paired inspiratory occlusions were applied to the subject while respiratory and electroencephalographic (EEG) data were recorded (Chan and Davenport, 2008). After each condition, participants rated the emotional and respiratory feelings experienced on the Self-Assessment Manikin (SAM) and the modified Borg scale, respectively.

2.4. Experimental emotion induction (affective picture series)

Emotional states were evoked by watching unpleasant and neutral pictures from the IAPS (Lang, 2008), a commonly used and standardized method for experimental emotion induction. The experienced emotional states during picture viewing are usually rated according to their hedonic valence and arousal. Thirty unpleasant pictures (high arousal and low valence) and thirty neutral pictures (low arousal and medium valence) were selected from the IAPS system. Pictures were displayed on a 71x40 cm monitor placed 2 meters in front of the participants. After the projection of a black screen for 1 minute, pictures from one set (unpleasant or neutral) were randomly presented for 10 seconds each, using experimental stimulus software (Presentation, Neurobehavioral Systems Inc.). The picture set was repeated four times resulting in a 20-minute sessions for each condition. Picture

hedonic valence and arousal were rated using a paper and pencil version of the SAM (Bradley and Lang, 1994) based on a 1 to 9 illustrated scale.

2.5. Inspiratory occlusions

Subjects were informed that respiration would be occasionally obstructed for a very short time and they were trained to breathe through the breathing circuit with and without inspiratory occlusions. Paired occlusions were applied every one to four inspirations according to a random algorithm. Occlusions were initiated manually by the researcher immediately after the onset of inspiration indicated by mouth pressure and airflow signals. The activation of the occlusion trigger initiated two occlusions within a single inspiration of 150 ms each separated by a 500 ms interval. A minimum of 64 inspiratory occluded breaths were recorded in each condition. A parallel marker signal was sent to the EEG computer. An occlusion valve produced the occlusion of the inspiratory port. Upon completion of each condition, i.e. unpleasant and neutral, subjects rated the intensity of perceived respiratory sensation on a modified Borg scale from 0 (nothing at all) to 10 (maximal).

2.6. Respiratory monitoring

Airflow was continuously recorded from a pneumotachograph connected to a differential pressure transducer connected to a demodulator (model MP-45, Validyne Engineering Corporation). Mouth pressure was recorded at the center of the non-rebreathing valve with a differential pressure transducer connected to a demodulator (model MP-45, Validyne Engineering Corporation). The mouth pressure and airflow signals were acquired by PowerLab hardware and analyzed with LabChart 7 software (ADInstruments). Since airflow and pressure signals were monitored in order to trigger inspiratory occlusions, only the respiratory rate was analyzed.

2.7. EEG monitoring

A scalp electrode cap (Quick-cap, Compumedics Neuromedical supplies) was positioned on the subject's head according to the International 10-20 system. Electrodes were filled with a conducting paste and impedance was kept to less than 5 kΩ. After skin preparation, two bipolar electrodes were placed above and below the left eye in order to record vertical eye EOG and electrode ear clips were attached to both ears. EEG activity was acquired and amplified by a SynAmp^2 system (Compumedics Neuroscan) using a sample rate at 1000 Hz, band-pass filter at 200 Hz to DC range, notch filter at 60

Hz and average referenced. Evoked potential analysis was performed using the Scan 4.3 software (Compumedics Neuroscan). Raw data were inspected visually and corrected for DC offset and EOG artefact (blinks and eye movements).

2.8. EEG analysis

2.8.1. RREP

Data were analyzed off-line. Epochs were extracted 100 ms pre- and 400 ms post-stimulus and averaged. Based on previous reports (Chan and Davenport, 2008), the RREP components were identified as: Nf, the first negative wave (latency = 25-45 ms) in the frontal region (electrodes F3 and F4); P1, the first positive wave (latency = 45-65 ms) in the centro-parietal region (electrodes CP3 and CP4); and N1, the second negative wave (latency = 85-125 ms) in the centro-lateral region (electrodes C3, Cz and C4). Analyses of RREP peaks were performed in the best derivation (electrode where the signal-to-noise is the best: no contamination, no DC shift of the signal baseline, presence of a RREP wave). If the quality of the signal was considered equivalent, F3 for Nf, CP3 for P1 and Cz for N1 were selected. The amplitudes of the averaged RREP peaks Nf, P1 and N1 elicited by the first occlusion and the amplitude of the averaged RREP peak N1 elicited by the second occlusion were compared between neutral and unpleasant conditions.

2.8.2 Gating RREP

The amplitude of the averaged RREP N1 peak of the first (S1) and second (S2) paired inspiratory occlusions were measured from the same recording site (electrode). The respiratory sensory gating has been described with the measure of the ratio S2/S1 (Chan and Davenport, 2008). In the present study, the ratio S2/S1 could not be analyzed in several cases because a DC shift occurred between the first and the second RREP leading to a positive value of N1S2. This effect is common with a short inter-stimulus interval and may be corrected by calculating manually a new baseline for the second RREP. In order to avoid a measurement bias by this method, we estimated the respiratory sensory gating by the difference between S2 and S1 amplitudes (S2-S1). The averaged DC shift between S1 and S2 being similar in neutral and unpleasant conditions in a same subject, testing the hypothesis H0 "$(S2\text{-}S1)_{neutral} = (S2\text{-}S1)_{unpleasant}$" suppresses the issue of the baseline DC shift.

2.9. Statistical analysis

Statistical analysis was performed using SPSS 21 (IBM software). Results are reported as median [min;max]. Medians of dependent variables (valence score, arousal score, respiratory rate, Borg scale score, RREP peaks latencies and amplitudes and difference score S2-S1) were compared between emotional conditions using the nonparametric Wilcoxon signed-rank test for related samples and between groups (independent variables: gender, conditions order) using the nonparametric Mann-Whitney U test for independent samples. Correlations between dependent variables and the Trait and State Anxiety scores were assessed using the nonparametric Spearman test. The value of alpha was 0.05.

3. Results

Observed variables are expressed as median and the minimal and maximal values (data in the square brackets).

3.1. Subjects

Thirteen subjects (6 males, 7 females) were retained for analysis; age 34 years [23;46], BMI 24 $kg.m^{-2}$ [20;35]. State and Trait anxiety scores were 31 [24;54] and 37 [33;49], respectively.

3.2. Valence and arousal ratings of IAPS pictures

Neutral pictures were rated according to SAM with medium valence (5 [3;8]) and low arousal (2 [1;4]) and unpleasant pictures with low valence (3 [1;6]) and high arousal (6 [2;9]) (figure 1). Although one subject rated neutral pictures as low valence and another one rated unpleasant pictures as medium valence, all subjects rated unpleasant pictures with a significantly lower valence (-2 [-4;-1]) and higher arousal (4 [2;6]) in comparison with neutral pictures (p=0.001).

3.3. Effect of IAPS pictures on breathing

Respiratory rate was significantly higher while viewing unpleasant versus neutral pictures series (11.5 brpm [10;18] versus 10 brpm [7;16]; p=0.016). There was no statistically significant difference in Borg scale ratings between neutral and unpleasant conditions (1 [0;4] versus 1 [0;3]; p=0.21).

3.4. Effect of IAPS pictures on the RREP elicited by the first occlusion

3.4.1. Nf and P1

The Nf was observed in 7 subjects (4 males and 3 females). Nf latency was 30 ms [26;40] in both conditions. There was no significant difference between conditions in Nf amplitude (table 1 and figure 2). The P1 was observed in 8 subjects (4 males and 4 females). P1 latency was 46 ms [30;70] and 46 ms [28;72] in neutral and unpleasant conditions, respectively. There was no between conditions difference in P1 latency and P1 amplitude (table 1 and figure 2).

3.4.2. N1 (S1)

The N1 for S1 was observed in 10 subjects (6 males and 4 females). N1 S1 latency was 100 ms [74;124] and 101 ms [74;124] in neutral and unpleasant conditions, respectively. N1 S1 amplitude was significantly decreased in the unpleasant condition (-3.37 µV [-4.62;-1.37]) in comparison with the neutral condition (-4.59 µV [-6.08;-1.36]; p=0.017) (table 1, figure 2 and figure 3).

3.5. Effect of IAPS pictures on the RREP peak N1 elicited by the second occlusion (S2)

The N1 S2 was observed in 9 subjects. N1 S2 latency was 100 ms [74;124] and 101 ms [74;124] in unpleasant and neutral conditions, respectively. There was no difference in N1 S2 amplitude between unpleasant (-0.26 µV [-3.24;2.36]) and neutral conditions (-0.7 µV [-1.54;3.6]; p=0.68) (table1, figure 3).

3.6. Effect of IAPS pictures on gating N1 (S2-S1)

The N1 difference score (S2-S1) was significantly lower in unpleasant condition (3.73 µV [0;5.82]) compared with neutral condition (4.79 µV [3;6.2]; p=0.038), suggesting decreased gating of the RREP N1 peak while viewing unpleasant pictures series (table 1, figure 2 and figure 3).

3.7. Effect of the conditions order, gender and anxiety states

Seven participants started the experiment with the neutral condition and 6 with the unpleasant condition. Results did not differ according to the order of experimental conditions or gender. State and Trait Anxiety scores did not correlate with IAPS pictures valence and arousal scores, respiratory rate, Borg scale score, RREP peaks amplitudes and latencies, and gating of N1.

4. Discussion

4.1. Effect of unpleasant emotions on RREP components

Results of the present study support the hypothesis that negative emotion affects the cortical processing and the neural gating of respiratory evoked sensory activity measured by the RREP. The RREP Nf and P1 peaks are thought to be exclusively related to the discriminative component of the respiratory sensory perception. Indeed, their amplitudes correlate with the stimulus magnitude (Davenport et al., 2007; Knafelc and Davenport, 1997, 1999) but not with attention (Chan and Davenport, 2009; Webster and Colrain, 2000b) nor with emotion (von Leupoldt et al., 2011; Von Leupoldt et al., 2010b), consistent with the present study. This suggests that the peripheral encoding of sensory signals and the initial cortical activations are not affected by emotion. The RREP third wave N1 is a function of both the discriminative and affective components of respiratory sensory perception (Davenport and Vovk, 2009). Its amplitude increases with attention to respiratory stimuli (von Leupoldt et al., 2010a; Webster and Colrain, 2000a, b) and, according to the results of the present study, decreases with unpleasant emotion. The decrease in N1 amplitude while viewing unpleasant pictures is likely related to a shift of subject's attention toward the non-respiratory emotional stimulus, i.e. IAPS pictures. The competitive effect of unpleasant IAPS pictures for attentional resources has previously been reported in other sensory modalities (Kenntner-Mabiala et al., 2008; Mini et al., 1995; Muller et al., 2008; Ring et al., 2013). Additionally, when attention is focused on the respiratory stimulus the amplitude of N1 S1 is not modified by viewing unpleasant IAPS pictures or by anxiety state (von Leupoldt et al., 2011; Von Leupoldt et al., 2010b). Interestingly, our findings as well as results from previous studies investigating neurophysiological substrates underlying the emotion-induced over-perception of sensations report a decrease in the brain activity related to the stimulus, which seems inconsistent with over-perception. Then, we hypothesized that unpleasant emotion might affect another mechanism involved in sensory perception, i.e. the sensory gating.

4.2. Effect of unpleasant emotions on RREP gating

The current study shows that experimental unpleasant emotion reduced the gating of respiratory sensations. The respiratory sensory gating was evaluated using the difference score between N1 S2 and N1 S1, which has been demonstrated to have a better reliability than the S2/S1 suppression ratio in the field of auditory research (Dalecki et al., 2011; Rentzsch et al., 2008; Smith et al., 1994). A decrease in gating - or "filtering" - redundant sensations leads to an excess in sensory information

arrival into the cortex. This may explain, at least in part, the increase in perception of respiratory sensations, i.e., over-perception, experienced during unpleasant emotion. Consistent with our results, Chan et al. have previously shown that high anxious compared to low anxious subjects displayed a *decreased* respiratory sensory gating (Chan et al., 2012). Interestingly, this was more closely related to an increased neural response to the second stimulus rather than a decreased response to the first stimulus in a paired inspiratory occlusion paradigm. A similar impact of anxiety on acoustic sensory and sensorimotor gating has also been reported (Hunter et al., 2011; Sanchez-Morla et al., 2008).

4.3. Anatomic and neurobiological speculations

The main subcortical anatomic site proposed for sensory gating is the thalamus. Indeed, inactivation of thalamic nuclei produces a deficit in somatosensory (Trageser and Keller, 2004), auditory sensory and sensorimotor gating (Krause et al., 2003; Wolf et al., 2010) in rats. In humans, exploratory data showed a deficit in somatosensory gating in patients with thalamic stroke (Staines et al., 2002). Furthermore, several studies have focused on a putative link between a neurodevelopmental defect of the thalamus and a deficit in sensory gating in schizophrenic patients (Patterson et al., 2008). The hippocampus is also an anatomic candidate for sensory gating (Bak et al., 2011; Grunwald et al., 2003; Schridde and van Luijtelaar, 2001) as neonatal hippocampus impairment leads to a deficit in sensory gating in rats (Broberg et al., 2007; Sandner et al., 2012; Swerdlow et al., 2012; Vohs et al., 2009). Both the thalamus and the hippocampus receive respiratory afferents. Thus, from an anatomical perspective, these neural substrates are good candidates to participate in the gating of respiratory sensations (Davenport and Vovk, 2009). The molecular basis for sensory gating (Guo et al., 2013; Ma and Leung, 2011; Richardson et al., 2011, 2013; Tsai et al., 2012) is proposed to be a tonic inhibition of sensory inputs by the GABAergic system. A deficit in the GABAergic transmission has been reported in animal models of anxiety and in human anxiety disorders (Engin et al., 2012). It might be induced by the action of epinephrine, a neuromodulator that is strongly released during emotional processes, directly on thalamic cells and/or via the prefrontal-thalamic system (Alsene and Bakshi, 2011; Alsene et al., 2011). Unpleasant IAPS pictures have been shown to activate the hippocampus as well as the prefrontal cortex (Aldhafeeri et al., 2012), suggesting a role for both structures in the modulation of the respiratory sensory gating observed in our study. The thalamus is not activated by

unpleasant IAPS pictures but it has strong interconnections with the amygdala, the anterior cingulate and the prefrontal cortex which are activated by viewing unpleasant pictures (Aldhafeeri et al., 2012). The decrease in the thalamic respiratory sensory gating might be responsible for an immediate over-perception of respiratory sensations whereas the decrease in hippocampus respiratory sensory gating might be involved in the memory of an increased perception of respiratory sensations.

Consistent with the link between anxiety and tachypnea, viewing unpleasant pictures increased the respiratory rate. The amygdala is an essential structure for respiratory response to stress (Bondarenko et al., 2014) although the exact neuronal pathway between amygdala and respiratory centers remain unknown. The central neural generator of respiration might be directly activated by the amygdala (Frysinger and Harper, 1989; Masaoka and Homma, 2004; Onimaru and Homma, 2007) through the effect of the norepinephrine (Viemari and Tryba, 2009) and/or orexin (Liu and Shen, 2010; Young et al., 2005; Zhang et al., 2009), two neuromodulators released during negative emotional experiences and able to bind receptors in the pre-Botzinger complex. However, in our study, we cannot exclude a participation of the cortical breathing command in response to the increase of respiratory sensations. In contrast to previous reports (Von Leupoldt et al., 2010b), the present study did not find any statistically significant increase in the perception of respiratory sensations while viewing unpleasant pictures. This might be due to the sample size and/or to differences in the experimental design such as ignored versus attended condition, different selection and presentation of pictures, less aversive respiratory stimulus, and different rating scales.

4.4. Clinical perspectives

In conclusion, viewing unpleasant pictures produced two effects on the RREP: a decrease in the N1 peak amplitude related to an attentional defect and a decrease in the gating of the RREP N1 peak. From the latter finding, it can be hypothesized that the over-perception of respiratory sensations experienced by certain patients could relate in part to an emotion-related decrease in respiratory sensory gating. A decreased respiratory gating might also provide a basis for the pathophysiology of the hyperventilation syndrome, a condition where patients display both severe dyspnea and chronic hyperventilation unexplained by an organic cause and suffer from profound alterations in quality of life (Chenivesse et al., 2014). Preliminary data have shown that a low intensity respiratory stimulus

leads to an abnormal activation of the insula cortex (Jack et al., 2010) - a brain region associated with dyspnea (Banzett et al., 2000; Peiffer et al., 2001) in these patients. If we assume that patients with hyperventilation syndrome experience unconscious negative emotions (LeDoux, 2014), we can speculate that the excessively perceived normal respiratory sensations may be due to a decrease in respiratory sensory gating. Studies of respiratory gating in patients with hyperventilation syndrome should answer this question. Of note, that negative emotions may affect the neural processing of central respiratory sensory gating paves the way for therapeutic interventions with drugs such as nicotinic acetylcholine receptor agonists (Chan and Davenport, 2010b) or meditation practices (Perlman et al., 2010; Zeidan et al., 2011) for the treatment of what is often called “emotional” dyspnea.

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Figure Legends

Figure 1

Valence and arousal SAM ratings of neutral and unpleasant IAPS picture series. The bold line is the median. The bottom and top of the box are respectively the first and third quartiles. The ends of the bars represent the minimum and maximum. ***p<0.01*

Figure 2

Amplitudes (µV) of the RREP peaks Nf, P1 and N1 (=S1) elicited by the first stimulus and difference score between S2 and S1 peak amplitudes (S2-S1) in neutral and unpleasant conditions. The band inside the box is the median. The bottom and top of the box are respectively the first and third quartiles. The ends of the bars represent the minimum and maximum. **p<0.05*

Figure 3

Averaged RREP elicited by paired inspiratory occlusions (first stimulus: plain lines, second stimulus: dotted lines) in unpleasant (black lines) and neutral (gray lines) emotional conditions (electrode C3, n=5). The time of 0 ms is the time of mouth pressure change produced by the inspiratory valve occlusion. N1 is the negative (upward) wave. The peaks Nf and P1 are not identifiable on this graph because the signal is from the electrode C3. The N1 elicited by the first stimulus (S1) has smaller amplitude in unpleasant condition compared with neutral condition. The N1 elicited by the second stimulus (S2) is similar in the two conditions. The difference score (S2-S1) is smaller in unpleasant condition compared with neutral condition.

Figure 1

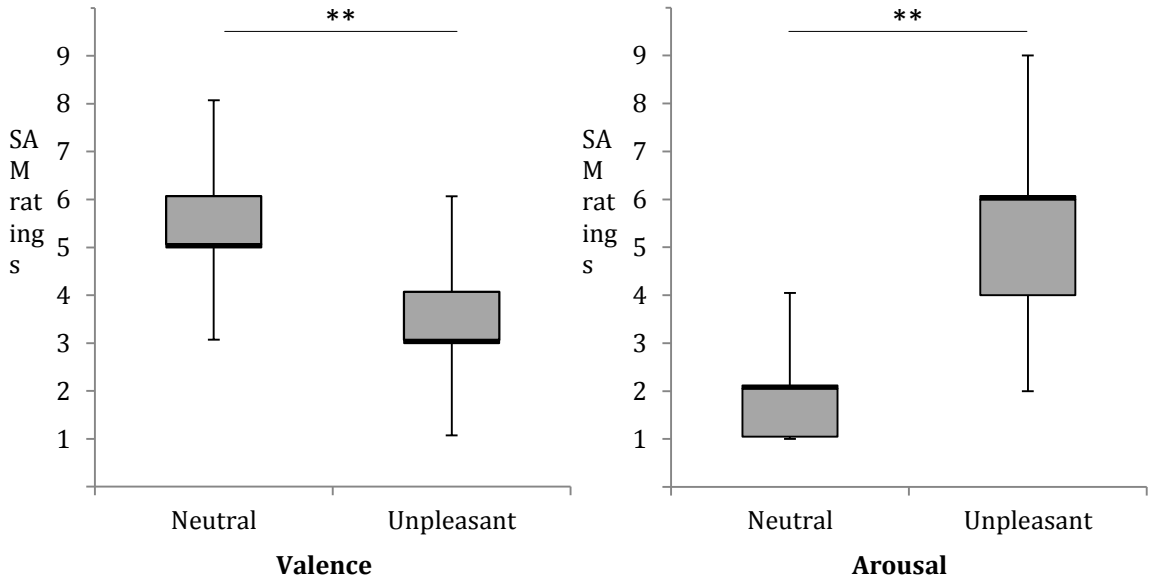

**
SAM ratings
9
8
7
6
5
4
3
2
1
Neutral
Unpleasant
Valence
**
SAM ratings
9
8
7
6
5
4
3
2
1
Neutral
Unpleasant
Arousal

Figure 2

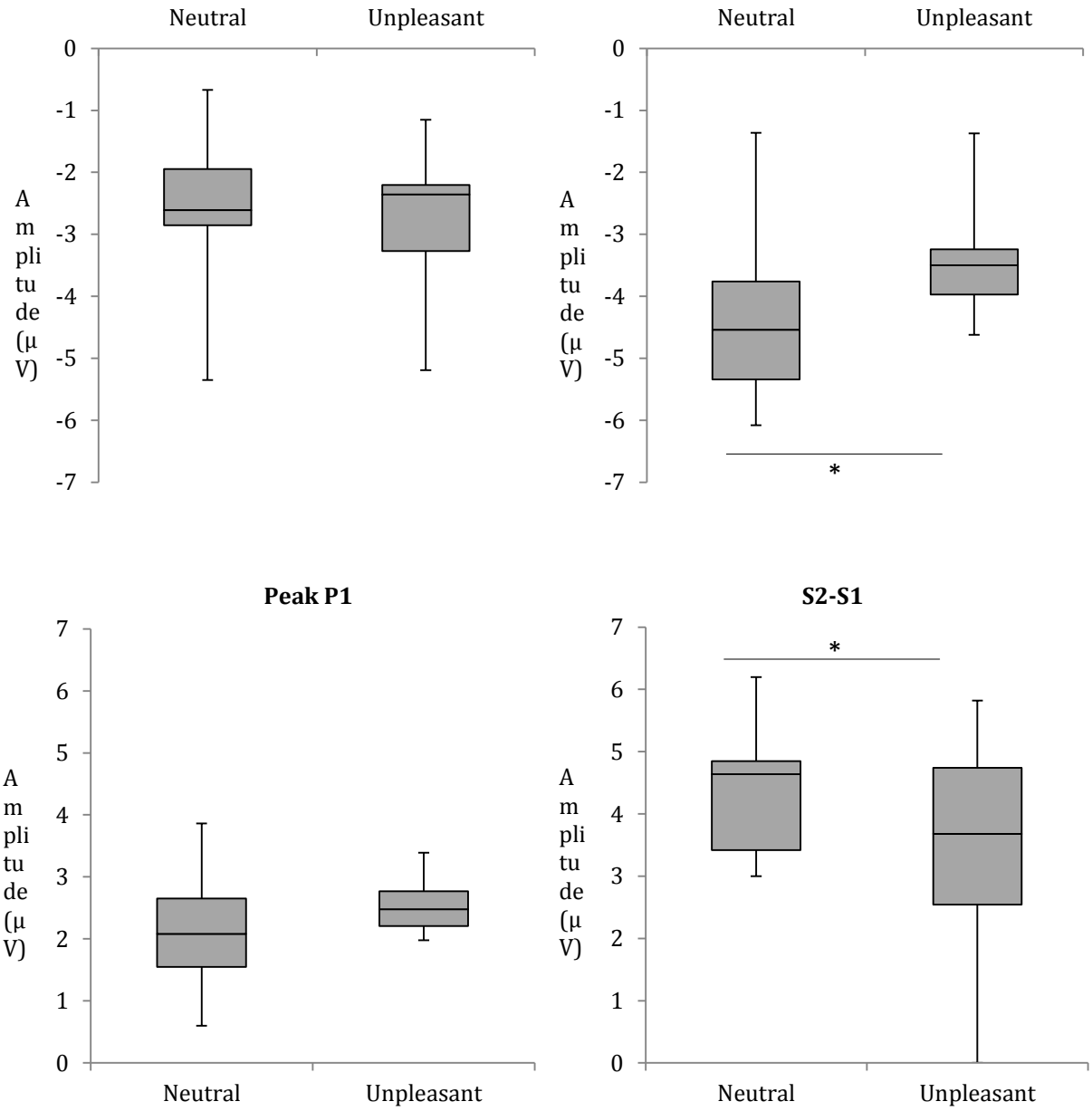
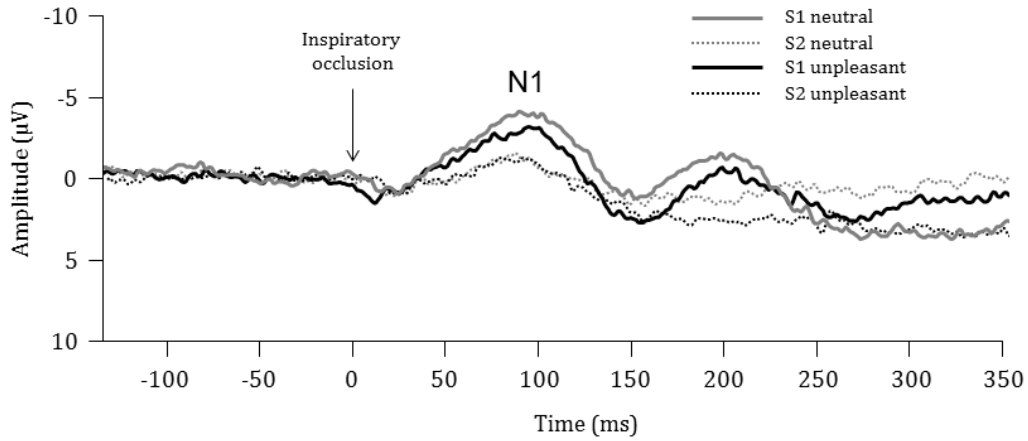

Neutral
Unpleasant
0
-1
-2
-3
-4
-5
-6
-7
Amplitude (µV)
*
Peak P1
S2-S1
7
6
5
4
3
2
1
0

Figure 3


-10
-5
0
5
10
Amplitude (μV)
Inspiratory occlusion
N1
S1 neutral
S2 neutral
S1 unpleasant
S2 unpleasant
-100
-50
0
50
100
150
200
250
300
350
Time (ms)